REMARKS

STATUS OF THE CLAIMS

Claims 1-7, 10-36 and 40-73 are pending as shown above and examined claims 34-36 and 40-43 remain rejected under 35 U.S.C. § 112, 1st paragraph (written description). As noted above, the listing of the claims provided above is for the Examiner's convenience and no amendments have been made to the claims.

35 U.S.C. § 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

The sole remaining rejection of claims 34-36 and 40-43 is alleged lack of written description.

It is alleged that the genus of fusion molecules, particularly the components of the fusions, encompassed by the claims is unduly broad. It was asserted that possession of the "large number" of fusions encompassed by the claims has not been demonstrated, on the grounds that the specification only "discloses" a fusion polypeptide that recognizes a site in VEGF and which fusion polypeptide comprises one of 5 enzymatic domains. (Final Office Action, page 3 last sentence). In addition, it was also asserted that Applicants' arguments were not persuasive, in part, because the components were argued "separately."

It is axiomatic that any written description inquiry is dependent on the particular facts of the case. *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991); *In re Wertheim*, 191 USPQ 90 (CCPA 1976). The facts that must be taken into account include the disclosure as a whole and the knowledge possessed by the skilled artisan at the time of filing, for example as established by reference to patents and publications available to the public prior to the filing date of the application. *See, e.g., In re Lukach*, 169 USPQ 795, 796 (CCPA 1971); *In re Lange*, 209 USPQ 288 (CCPA 1981). That which is not new need not be described in detail. *See, e.g., Capon v. Eshhar* 76 USPQ2d 1078 (Fed. Cir. 2005).

Thus, the proper standard for determining satisfaction of the written description involves reviewing the disclosure as a whole, taken together with available knowledge, to determine whether the specification as-filed evinces possession of the claimed subject matter to the skilled artisan. Any written description inquiry that does not completely or accurately assess the particular disclosure of the specification and determine the state of the field is necessarily flawed.

Throughout prosecution of the instant case, the Office has failed to consider both the disclosure of the as-filed specification as a whole and the knowledge possessed by the skilled artisan at the time of filing. Instead, the Office appears to have considered only the Examples and Figures, and has failed to acknowledge the known state of the field (*e.g.,* as evidenced by published information). Consequently, the adequacy of Applicants' written description has not been properly assessed and the rejection cannot be sustained.

The Office's assessment that the specification in question "discloses" only that which is exemplified can be found throughout both the non-Final and Final Office Actions (*see,* Final Office Action, page 3, last paragraph; page 4, first paragraph; page 8, second paragraph; page 9, first and second paragraphs (emphasis added)):

> The specification **discloses** a fusion polypeptide comprising a DBD [DNA-binding domain] that recognizes target sequence in the human VEGF gene, which is alternatively fused to BAF155, MBD1, MBD2, MDB3, DNMT, and KRAB (e.g., Figs. 6-7; Examples 2-13).
>
> The **disclosed** embodiments are directed exclusively to DNA modification, while the claims encompass a genus that includes both DNA or histone covalent modification. There are no embodiments **disclosed** of structures or functional fragment [*sic*] of structures that function to covalently modify histones.
>
> Notably the specification **identifies** structures that are non-enzymatic components of chromatin remodeling complexes (*e.g.,* MBD1, MBD2, MBD3, DNMT and KRAB; Examples 2-13, Figs. 6-7).
>
> In other words, not a single embodiment is **disclosed** of a fusion molecule structure that functions to covalently modify histones.
>
> In addition, the specification does not **identify** a single fusion molecule where the DNA binding domain is a non-protein (e.g., chemical agent or nuclei [*sic*] acid), but that is linked to an enzymatic component or functional fragment thereof, and that effectuates chromatin remodeling.

Time and time again, the Office ignores what is disclosed in the background, summary, detailed description and original claims, asserting instead that only the Examples and Figures should be consulted to assess adequacy of disclosure.

However, when the actual disclosure and state of the art regarding Applicants' particular case are properly assessed, it is clear that the written description requirement has been met, and possession of the claimed subject matter has been conveyed.

Indeed, as repeatedly noted, the as-filed specification contains literal disclosure of known enzymatic components of chromatin remodeling complexes (*see, e.g.,* Background as well as pages 32-42 describing, in detail, enzymatic chromatin remodeling complexes that covalently modify histones) as well as known non-protein DNA binding domains (*see, e.g.,* page 5, lines 29-30; page 30, lines 5-23 describing non-protein DBDs such as triplex-forming nucleic acids, intercalators, antibiotics, and minor groove binders). Moreover, the as-filed specification literally discloses the novel claimed fusion molecules (*see, e.g.,* pages 7, lines 23-31; page 8, lines 1-9 and 18-21; pages 32-42). Simply put, there is literal disclosure in the specification of every embodiment encompassed by the claims.

In the instant case, the Office has taken into account only that which is exemplified. When viewed as a whole, Applicants' disclosure literally discloses every embodiment falling within the scope of the claims. Not only have Applicants shown possession of the individual components of the claimed fusion molecules (*see, e.g.,* Background and pages 32-42 detailing known chromatin remodeling complexes that covalently modify histones and page 30 detailing non-protein DNA binding domains), they have evinced possession of that which is new – namely fusing a DNA binding domain to a histone methyl transferase, a histone kinase, a histone phosphatase, a histone ubiquitinating enzyme, a histone de-ubiquitinating enzyme or a histone protease.

Disclosure, not exemplification, is what is relevant to the written description inquiry and, in the case at hand, there is ample disclosure demonstrating possession of the claimed genus. To require exemplification of actual, multiple embodiments is contrary to all established precedent and the rejection should be withdrawn.

1. Possession of the Claimed Genus Has Been Established

As noted above and throughout prosecution (including the Pre-Appeal Brief Conference Arguments filed November 14, 2005), the as-filed specification contains ample description regarding the claimed fusion molecules. This includes literal description of the known components (known histone modifying enzymes and known DNA-binding molecules) as well as proper citations to references indicating what was known to those skilled in the art (again, the particular enzymatic components of the recited chromatin remodeling complexes and various known DNA binding domains). More importantly, the specification teaches that which is new,

i.e., how to fuse these known DNA binding domains to known chromatin remodeling proteins to form the novel and unobvious fusion molecules of the claims.

(a) The As-Filed Specification Describes the Claimed Genus Throughout Its Scope

As noted above, the Office has repeatedly asserted that no structures of non-protein fusion molecules or enzymatic chromatin remodeling complexes are described and that the art cannot supplement the allegedly inadequate disclosure (*see, e.g.*, pages 5 and 7 of the Final Office Action):

> The specification does not provide any structures comprising non-protein fusion molecules (e.g., genus of molecules encompassed by claim 40). Furthermore, knowledge in the art does [*sic*][1] supplement the instant disclosure's omission of a sufficient description. For example, "In contrast to the relative wealth of information about the large number of acetyltransferases and deacetylases, relatively little is known about the enzymes that generate other histone modifications." [citation omitted] ...
>
> Given the enormous breadth of the fusion molecules, comprising DNA binding domains and enzymatic components or chromatin remodeling complexes, including functional fragments thereof, encompassed by the rejected claims, including non-protein-protein fusion molecules, and given the limited description in the instant specification of such fusion molecules, the skilled artisan would not be able to envision a sufficient number of specific embodiments to described [*sic*] the broadly claimed genus. Therefore, the skilled artisan would reasonably have concluded that applicants were not in possession of the claimed invention.
>
> The instant specification provides insufficient description of the essential/critical structures encompassed by the broadly claimed genus of fusion molecules.

In fact, the assertions that the specification is defective and that art available at the time of filing cannot be used to supplement the disclosure are in error.

As repeatedly noted, the as-filed specification amply discloses structures of non-protein DNA binding domains (*e.g.*, page 30 of the as-filed specification). In addition, the as-filed specification also provides structures of various chromatin remodeling proteins as claimed, including, for example, histone kinases (*see, e.g.*, page 3, line 23 and citing Sassone-Corsi et al. (1999), Ref. CI-1 of IDS filed June 27, 2002) and histone methyltransferases (*see, e.g.*, page 2,

[1] Applicants assume "does not" was intended

line 31 citing Rea et al. (2000), Ref. CF-1 of IDS filed June 27, 2002 and the detailed description on pages 32-42, particularly page 33, of proteins such as Su(Var)3-9 that were known at the time of filing to be histone methyltransferases).

Furthermore, contrary to the assertion in the Final Office Action, it is completely proper to supplement the specification's disclosure using references available at the time of filing. *See, e.g., In re Lukach*, 169 USPQ 795, 796 (CCPA 1971); *In re Lange*, 209 USPQ 288 (CCPA 1981). Indeed, a patent specification need not recite and preferably omits that which is not new. *See, e.g., Loom Co. v. Higgins,* 105 U.S. 580, 585-86 (1882); *In re Wands,* 858 F.2d 731 (Fed. Cir. 1988) and *In re Gay,* 309 F.2d 769, 774 (CCPA 1962) pointing out that "not every last detail [of an invention need] be described [in a specification], else patent specifications would turn into production specification, which they were never intended to be." See also *Capon v. Eshhar* 76 USPQ2d 1078 (Fed. Cir. 2005) for a recent explication of this doctrine in the biotechnology context.

In the present case, structures of various exemplary histone modifying proteins were known at the time of filing and citations to these proteins are contained in the as-filed specification (*see, e.g.,* Sassone-Corsi et al. (1999) and Rea et al. (2000) cited in the specification and disclosed as references CI-1 and CF-1, respectively, in the IDS filed June 27, 2002, which disclose the structure of histone kinases and histone methyltransferases).

Indeed, SNF-1, which is described in detail in the specification, was known at the time of filing to be a histone kinase (*see, also,* Lo et al. (2001) *Science* 293(5532):1142-1146, Ref C4 of IDS filed herewith). Additional histone modifying enzymes (and their sequences) were available to the public well before the application was filed in 2001. By way of example, histone phosphatases such as PP2A were described as early as 1988 (*see, e.g.,* Usui et al. (1988) *J. Biol. Chem.* 263:3752-3761, Ref C5 of IDS filed herewith and Zhao (1994) *Biochem Mol Biol Int* 34(5):1027-1033), Ref C6 of IDS filed herewith). Histone proteases, histone ubiquitinating enzymes and histone de-ubiquitinating enzymes were described in the mid-1990s (*see, e.g.,* Goffeau et al. (1996) *Science* 274:546-547, Ref C2 of IDS filed herewith; Kaiser et al. (1994) *J. Biol. Chem.* 269:8797-8802, Ref C3 of IDS filed herewith; Cai (1999) *Proc Nat'l Acad Sci USA* 96(6):2828-2833, Ref C1 of IDS filed herewith).

Thus, those of skill in the art would have been aware of the histone modifying enzymes described in the previous paragraph, as of the filing date. Applicants have also provided

evidence that the claimed DNA-binding domains, both protein and non-protein, were known in the art at the time of filing. *See* Applicants' Response dated April 19, 2005 at pages 13-14. It is unreasonable to assert that this known information must be set forth *verbatim* in the specification.

It is also unreasonable to assert that the claims must recite some kind of "essential" or "critical" structure encompassed by the claims. (*See,* page 7 of the Final Office Action, reproduced above). The nature of the claimed fusion molecules is such that they cannot be adequately presented by recitation of a single structure, even though the as-filed specification provides ample description in this regard. Broad, pioneering claims are not *per se* inadequately described. In fact, all the critical features of the claimed, pioneering fusion molecules have been described.

Furthermore, Applicants submit that the allegation that "relatively little" is known about certain histone modifying enzymes is irrelevant to the instant written description inquiry. First of all, it was not specified what is not known about these enzymes. Their structure and/or function may be well characterized but "relatively little known" about such things as their mechanism of action.

In sum, given the disclosure of the specification, one of skill in the art would clearly envision the allegedly enormous breadth of the claims.[2] Indeed, the Office has envisioned such embodiments. *See, e.g.,* page 4, first paragraph of the Final Office Action, noting that the specification points out that "chromatin remodeling can occur through DNA or histone covalent modification" as encompassed by the claims.[3]

(b) The Case Law Supports a Finding that the As-Filed Specification Describes the Claimed Subject Matter

Because literal description of numerous representative fusion molecules is present in the specification as filed, the Office cannot rely on *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991), *Lockwood v. American Airlines, Inc.*, 41 USPQ2d 1961 (Fed. Cir. 1997) and

[2] Applicants note also that the breadth of a claim has no relationship to the adequacy of its written description

[3] Page 5 of the Final Office Action provides a specific example of the Office's vision of a claimed embodiment. Therein it is stated that Pham *et al.* show histone ubiquitin[ating] activity for $TAF_{II}250$. Thus, a fusion between $TAF_{II}250$ and a DNA-binding domain represents an embodiment that has been envisioned.

University of California v. Eli Lilly and Co., 43 USPQ2d 1398 (Fed. Cir. 1997) to try to show that the claimed subject matter is not adequately described.

In *Vas-Cath,* the Federal Circuit determined that the written description was in fact satisfied because the drawings did not have to exclude all diameters other than those within the claimed range. *Vas-Cath,* at 1119. Therefore, *Vas-Cath* actually supports a finding of adequate written description where the specification includes a disclosure of all possible fusion molecules.

In *Lockwood,* the written description requirement was analyzed in order to determine if the patentee was entitled to the benefit of a previous filing date for claims directed to particular automated sales terminals. The Federal Circuit reiterated the fact-dependent nature of the written description inquiry and, on the particular facts, held that possession was not shown because that which was claimed in the patent was not disclosed in an earlier application. *Lockwood,* at 1964. However, *Lockwood* contains a completely different fact-pattern than that found in the instant case (priority claim vs. adequacy of original disclosure/claims). Lockwood's claims failed to satisfy the written description requirement because an intervening application was held not to describe an terminal containing a video disc player. By contrast, and unlike *Lockwood,* Applicants' as-filed specification contains literal description of the claimed subject matter.

Thus, under both *Lockwood* and *Vas-Cath,* Applicants have demonstrated possession of the claimed subject matter, thereby fully satisfying the written description requirement.

As with *Lockwood*, the fact-pattern in *Eli Lilly* is completely different than that of the present case. In *Lilly,* the claims were directed to novel insulin-encoding sequences which were not disclosed in (or known prior to the filing of) the as-filed specification. In contrast, the pending claims are directed to novel fusion molecules that are literally described in the specification and whose components were described in the specification and known in the art. Therefore, the findings in *Eli Lilly* have no bearing on the facts of the present application.

Federal Circuit decisions that are more germane to the case at hand are *Union Oil Co. of California v. Atlantic Richfield Co.*, 208 F.3d 989, 54 USPQ2d 1227 (Fed. Cir. 2000) and *Capon v. Eshhar* 76 USPQ2d 1078 (Fed. Cir. 2005). Applicants note that both *Union Oil* and *Capon* are more recent than *Vas-Cath, Lockwood* and *Eli Lilly.*

In *Union Oil v. Atlantic Richfield*, the Federal Circuit made clear that the specification need **not** describe the exact chemical composition of every claimed combination, adding that neither the Patent Act nor case law requires such detailed disclosure (*see, Union Oil,* at 1223):

> Appellant refiners assert that the specification does not describe the exact chemical component of each combination that falls within the range claims of the '393 patent. However, neither the Patent Act nor the case of this court requires such detailed disclosure. ...
>
> The inquiry for adequate written description simply does not depend on a particular claim format, but rather on whether the patent's description would show those of ordinary skill in ... art that the inventors possessed the claimed invention at the time of filing.

In *Capon v. Esshar,* the Federal Circuit completely rejected the notion that the specification must describe information (*e.g.,* sequence data) that is either known or can readily be determined based on scientific facts (*Capon* at page 1085, emphasis added):

> The "written description" requirement must be applied in the context of the particular invention and the state of the knowledge. The Board's rule that the nucleotide sequences of the chimeric genes must be fully presented, although the nucleotide sequences of the component DNA are known, is an inappropriate generalization. ...
>
> The "written description" requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution.

The holding in *Capon* is particularly relevant to the instant case because the fact pattern in *Capon* is highly analogous to the fact pattern in the case at issue. In *Capon*, the Federal Circuit held that the precise sequence of a chimeric (fusion) antibody need **not** be described because the components were well known.

The assertion in the instant case that Applicants are required to provide multiple examples of particular fusion molecules, when each of the components (DNA binding domains that bind to particular target sites and enzymatic portion of the recited chromatin remodeling complexes), as well as methods of making fusion proteins, were well known and described in the specification as-filed, is inconsistent with the requirements of the first paragraph of Section 112.

Contrary to the assertions in the Final Office Action, and as the Federal Circuit confirmed in *Capon*, the written description requirement is satisfied when each component of the fusion molecule was well known and described and when methods for making fusion molecules are

well known in the art and described in the specification. Applicants have clearly evinced possession of the components of the claimed fusion molecules and, accordingly, have satisfied the written description requirement.

Moreover, Applicants also amply describe that which is new, *i.e.,* fusing a DNA binding domain to one of the chromatin remodeling proteins recited in the claims. Thus, the disclosure of the specification as filed more than satisfies the written description requirement with respect to the pending claims; and the notion that the specification provides "sufficient information in order for a person of skill in the art to construct such a product," but somehow fails to describe that product is completely at odds with not only *Capon* but with every case, rule and guideline relating to the written description requirement.

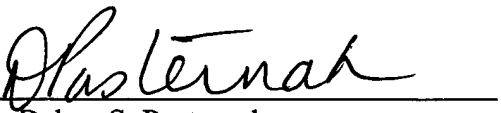
Plainly, clear description is present in the original claims and specification, and the written description requirement has therefore been satisfied. As result, the rejection cannot be sustained.

CONCLUSION

For the reasons state above, Applicant respectfully submits that the pending claims define an invention that is novel, non-obvious, fully enabled and described by the specification. Accordingly, Applicant requests that the rejection of the claims be withdrawn, and that the application proceed to allowance.

Respectfully submitted,

Date: June 5, 2006

By: 

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